AMENDMENTS TO THE CLAIMS

This listing of claims will replace all prior versions, and listings of claims in the application. Please amend claims 1, 4-19, 11-13, 16-18, 20, 23-27, 29, 32-33, 35-36, 38-50, 53-55, 58-59, and 62-65 as follows. Please cancel claims 10, 14, 15, 19, 21, 22, 28, 30, 31, 34, and 37.

1. (currently amended) A composition ~~phospholipid nanovesicle incorporating a polypeptide~~ comprising

a phospholipid, wherein the phospholipid is ~~dioleoyl phosphatidylserine~~ dioleoylphosphatidylserine (DOPS),

an isolated saposin C-related polypeptide, wherein the polypeptide is selected from the group consisting of: (a) a polypeptide having an amino acid sequence at least 95 percent identical to SEQ ID NO: 2; and (b) a polypeptide having an amino acid sequence identical to SEQ ID NO: 2; and

a pharmaceutically acceptable carrier;

wherein the polypeptide retains plasma membrane affinity;

wherein the phospholipid forms a nanovesicle incorporating the polypeptide;

and wherein the nanovesicle incorporating the polypeptide exhibits anti-tumor activity.

2. (canceled)

3. (canceled)

4. (currently amended) The composition of claim 1, wherein the molar ratio of the polypeptide to the phospholipid is in the range from about 1:1 to about 1:50.

5. (currently amended) The composition of claim 1, wherein the molar ratio of the ~~saposin C related~~ polypeptide to the phospholipid is in the range from about 1:1 to about 1:10.

6. (currently amended) The composition of claim 1 wherein the composition is capable of inducing apoptosis in hyper-proliferating cells, wherein the hyper-proliferating cells are selected from the group consisting of tumor cells and cancer cells.

7. (currently amended) The composition of claim 1, wherein the polypeptide comprises at least [[15]] 25 contiguous amino acids of SEQ ID NO: 2.

8. (currently amended) The composition of claim [[7]] 1, wherein the mass ratio of the polypeptide to the phospholipid is in the range from about 15:1 to about 3:10.

9. (withdrawn; currently amended) A method for modulating the distribution of an inner leaflet component in a plasma membrane of a hyper-proliferating cell of a subject comprising administering to ~~said~~ the subject a therapeutically effective amount of the ~~agent~~ composition of claim 1;

wherein the inner leaflet component is phosphatidylserine; and

wherein the hyper-proliferating cell is selected from the group consisting of a tumor cell and a cancer cell.

10. (canceled)

11. (withdrawn; currently amended) The method of claim [[10]] 9, wherein ~~said~~ the phosphatidylserine ~~or structural analog thereof~~ is dioleoylphosphatidylserine.

12. (withdrawn; currently amended) The method of claim 9, wherein the distribution of ~~said~~ the inner leaflet component in the outer leaflet of ~~said~~ the plasma membrane is altered.

13. (withdrawn; currently amended) The method of claim [[12]] 9, wherein the concentration of ~~said~~ the inner leaflet component in ~~said~~ the outer leaflet is increased.

14. (canceled)

15. (canceled)

16. (withdrawn; currently amended) The method of claim 9, wherein ~~said~~ the method promotes cell death of the hyper-proliferating cell.

17. (withdrawn; currently amended) A method of modulating tumor volume in a subject, ~~said~~ the method comprising administering a therapeutically effective amount of the ~~agent~~ composition of claim 1.

18. (withdrawn; currently amended) The method of claim 17, wherein ~~said agent~~ the composition promotes cell death in hyper-proliferating cells, wherein the hyper-proliferating cells are selected from the group consisting of tumor cells and cancer cells.

19. (canceled)

20. (withdrawn; currently amended) The method of claim [[19]] 18, wherein ~~said~~ the cancer cells are selected from the group consisting of sarcoma, neuroblastoma, breast carcinoma, and squamous cell carcinoma cells.

21. (canceled)

22. (canceled)

23. (withdrawn; currently amended) The method of claim 17, wherein ~~said~~ the subject is a mammal.

24. (withdrawn; currently amended) The method of claim 23, wherein ~~said~~ the mammal is a human.

25. (withdrawn; currently amended) The method of claim 17, wherein ~~said~~ the tumor volume decreases.

26. (withdrawn; currently amended) The method of claim 17, wherein the molar ratio of ~~said~~ the polypeptide to ~~said inner leaflet component~~ the phospholipid is in the range from about 1:1 to about 1:50.

27. (withdrawn; currently amended) The method of claim 26, wherein the molar ratio of ~~said~~ the polypeptide to ~~said inner leaflet component~~ the phospholipid is in the range from about 1:1 to about 1:10.

28. (canceled)

29. (withdrawn; currently amended) A method of treating a cancer in a subject, ~~said~~ the method comprising administering a therapeutically effective amount of the ~~agent~~ composition of claim 1.

30. (canceled)

31. (canceled)

32. (withdrawn; currently amended) The method of claim 29, wherein the molar ratio of ~~said~~ the polypeptide to ~~said inner leaflet component~~ the phospholipid is in the range from about 1:1 to about 1:50.

33. (withdrawn; currently amended) The ~~agent~~ method of claim 32, wherein the molar ratio of ~~said~~ the polypeptide to ~~said inner leaflet component~~ the phospholipid is in the

range from about 1:1 to about 1:10.

34. (canceled)

35. (withdrawn; currently amended) The method of claim 29, wherein ~~said agent~~ the composition promotes cell death in hyper-proliferating cells, wherein the hyper-proliferating cells are selected from the group consisting of tumor cells and cancer cells.

36. (withdrawn; currently amended) The method of claim 35, wherein ~~said~~ the cell death occurs through apoptosis.

37. (canceled)

38. (withdrawn; currently amended) The method of claim [[37]] 35, wherein ~~said~~ the cancer cells are selected from the group consisting of sarcoma, neuroblastoma, breast carcinoma, and squamous cell carcinoma cells.

39. (withdrawn; currently amended) The method of claim 29, wherein ~~said~~ the subject is a mammal.

40. (withdrawn; currently amended) The method of claim 39, wherein ~~said~~ the mammal is a human.

41. (withdrawn; currently amended) The method of claim 29, wherein ~~said agent~~ the composition is administered enterally, parenterally, subcutaneously, intravenously, intraperitoneally, or topically.

42. (withdrawn; currently amended) The method of claim 29, wherein multiple doses of ~~said agent~~ the composition are administered to ~~said~~ the subject.

43. (withdrawn; currently amended) The method of claim 29, wherein a single dose of ~~said agent~~ the composition is administered to ~~said~~ the subject.

44. (currently amended) An anti-tumor ~~composition~~ agent comprising a nanovesicle prepared by

(a) ~~combining~~ preparing a composition ~~comprising~~ that comprises (i) a dried inner leaflet component, wherein the inner leaflet component ~~comprises~~ is a phosphoplipid, wherein the phospholipid is ~~dioleoyl-phosphatidylserine~~ dioleoylphosphatidylserine (DOPS) and (ii) a dried and isolated prosaposin-related polypeptide;

wherein the polypeptide has an amino acid sequence selected from the group consisting of the amino acid sequence set forth in SEQ ID NO: 1, the amino acid sequence that is at least

95 percent identical to SEQ ID NO: 1, the amino acid sequence set forth in SEQ ID NO: 2, and the amino acid sequence that is at least 95 percent identical to SEQ ID NO:2 and wherein the polypeptide retains plasma-membrane affinity;

wherein the molar ratio of the polypeptide to the ~~inner leaflet component~~ dioleoylphosphatidylserine in the composition is in the range from 1:1 to 1:25;

in a pharmaceutically acceptable carrier;

(b) treating the ~~suspension of inner leaflet component and prosaposin related polypeptide~~ composition to form a nanovesicle;

wherein the nanovesicle formed has a diameter in the range 10 to 800 nm;

and wherein the composition is capable of inducing apoptosis in hyper-proliferating cells, wherein the hyper-proliferating cells are selected from the group consisting of tumor cells and cancer cells.

45. (currently amended) The anti-tumor ~~composition~~ agent of claim 44, wherein the mass ratio of the polypeptide to the dioleoylphosphatidylserine is approximately 5:1.

46. (currently amended) The anti-tumor ~~composition~~ agent of claim 44, wherein the mass ratio of the polypeptide to the dioleoylphosphatidylserine is approximately 15:7.

47. (currently amended) The anti-tumor ~~composition~~ agent of claim 44, wherein the mass ratio of the polypeptide to the dioleoylphosphatidylserine is in the range from about 15:1 to about 3:10.

48. (currently amended) The anti-tumor ~~composition~~ agent of claim 44, comprising approximately 10 μM polypeptide and approximately 30 μM dioleoylphosphatidylserine.

49. (currently amended) The anti-tumor ~~composition~~ agent of claim 44, comprising approximately 10 μM polypeptide and approximately 70 μM dioleoylphosphatidylserine.

50. (currently amended) A composition consisting essentially of an anionic phospholipid nanovesicle consisting of ~~dioleoyl phosphatidylserine~~ dioleoylphosphatidylserine (DOPS) embedded with a biologically active saposin C-related polypeptide, wherein the polypeptide comprises an amino acid sequence that ~~(i)~~ has at least 95% sequence identity to the amino acid sequence of SEQ ID NO:2; and a pharmaceutically acceptable carrier; wherein the phospholipid nanovesicle exhibits anti-tumor activity.

51. (canceled)

52. (canceled)

53. (currently amended) The composition of claim 50, wherein the molar ratio of the polypeptide to the phospholipid is in the range from about 1:1 to about 1:50.

54. (currently amended) The composition of claim 50, wherein the molar ratio of the polypeptide to the phospholipid is in the range from about 1:1 to about 1:10.

55. (currently amended) The composition of claim 50 wherein the composition is capable of inducing apoptosis in hyper-proliferating cells upon contact, wherein the hyper-proliferating cells are selected from the group consisting of tumor cells and cancer cells.

56. (canceled)

57. (canceled)

58. (withdrawn; currently amended) A process for the manufacture of a pharmaceutical ~~composition~~ agent comprising the steps of:

(a) ~~combining~~ preparing a composition ~~comprising~~ that comprises (i) an inner leaflet component, wherein the inner leaflet component is a phospholipid ~~selected from the group consisting of phosphatidylserine, phosphatidylethanolamine and structural analogs thereof,~~ wherein the phospholipid is dioleoylphosphatidylserine (DOPS) and (ii) a prosaposin-related polypeptide, wherein the polypeptide is selected from the group consisting of: (a) a polypeptide having an amino acid sequence at least 95 percent identical to SEQ ID NO: 2; and (b) a polypeptide having an amino acid sequence identical to SEQ ID NO: 2 and wherein the polypeptide retains plasma-membrane affinity;

~~wherein the polypeptide has an amino acid sequence selected from the group consisting of the amino acid sequence set forth in SEQ ID NO:1, a biologically active variant of the amino acid sequence set forth in SEQ ID NO:1, the amino acid sequence set forth in SEQ ID NO:1 having one or more conservative substitutions, the amino acid sequence set forth in SEQ ID NO:2, a biologically active variant of the amino acid sequence set forth in SEQ ID NO:2, and the amino acid sequence set forth in SEQ ID NO:2 having one or more conservative substitutions and wherein the polypeptide retains plasma membrane affinity;~~

in a pharmaceutically acceptable carrier;

(b) treating the ~~suspension of inner leaflet component and prosaposin related polypeptide~~ composition to form a nanovesicle;

wherein the nanovesicle formed exhibits anti-tumor activity.

59. (currently amended) A pharmaceutical ~~composition~~ agent comprising nanovesicles prepared by

(a) ~~combining~~ preparing a composition ~~comprising~~ that comprises (i) an inner leaflet component, wherein the inner leaflet component ~~comprises dioleoyl phosphatidylserine~~ is dioleoylphosphatidylserine (DOPS) and (ii) a prosaposin-related polypeptide;

wherein the polypeptide has an amino acid sequence selected from the group consisting of the amino acid sequence set forth in SEQ ID NO: 1, the amino acid sequence that is at least 95 percent identical to SEQ ID NO: 1, the amino acid sequence set forth in SEQ ID NO: 2, and the amino acid sequence that is at least 95 percent identical to SEQ ID NO:2 and wherein the polypeptide retains plasma-membrane affinity;

in a pharmaceutically acceptable carrier;

(b) treating the ~~suspension of inner leaflet component and prosaposin related polypeptide~~ composition to form a nanovesicle;

wherein the nanovesicle formed exhibits anti-tumor activity.

60. (canceled)

61. (canceled)

62. (currently amended) The pharmaceutical ~~composition~~ agent of claim 59, wherein the molar ratio of the polypeptide to ~~dioleoyl phosphatidylserine~~ the dioleoylphosphatidylserine (DOPS) is in the range from about 1:1 to about 1:50.

63. (currently amended) The pharmaceutical ~~composition~~ agent of claim 59, wherein the nanovesicle has a diameter in the range 0.01 to 1 μm.

64. (withdrawn; currently amended) A process for the manufacture of a pharmaceutical ~~composition~~ agent comprising the steps of:

(a) ~~combining~~ preparing a composition ~~comprising~~ that comprises (i) a dried inner leaflet component, wherein the inner leaflet component is ~~phosphatidylserine or a structural analog thereof~~ dioleoylphosphatidylserine and (ii) a dried and isolated prosaposin-related polypeptide, wherein the polypeptide is selected from the group consisting of: (a) a polypeptide having an amino acid sequence at least 95 percent identical to SEQ ID NO: 2; and (b) a

polypeptide having an amino acid sequence identical to SEQ ID NO: 2 and wherein the polypeptide retains plasma-membrane affinity;

~~wherein the polypeptide has an amino acid sequence selected from the group consisting of the amino acid sequence set forth in SEQ ID NO:1, the amino acid sequence set forth in SEQ ID NO:1 having one or more conservative substitutions, the amino acid sequence set forth in SEQ ID NO:2, and the amino acid sequence set forth in SEQ ID NO:2 having one or more conservative substitutions and wherein the polypeptide retains plasma membrane affinity;~~

wherein the molar ratio of the polypeptide to the inner leaflet component in the composition is in the range from 1:1 to 1:25;

in a pharmaceutically acceptable carrier;

(b) treating the ~~suspension of inner leaflet component and prosaposin related polypeptide~~ composition to form a nanovesicle;

wherein the nanovesicle formed has a diameter in the range 10 to 800 nm and exhibits anti-tumor activity.

65. (currently amended) A pharmaceutical ~~composition~~ agent comprising nanovesicles prepared by

(a) ~~combining~~ preparing a composition ~~comprising~~ that comprises (i) a dried inner leaflet component, wherein the inner leaflet component ~~comprises dioleoyl phosphatidylserine~~ is dioleoylphosphatidylserine (DOPS) and (ii) a dried and isolated prosaposin-related polypeptide;

wherein the polypeptide has an amino acid sequence selected from the group consisting of the amino acid sequence set forth in SEQ ID NO: 1, the amino acid sequence that is at least 95 percent identical to SEQ ID NO: 1, the amino acid sequence set forth in SEQ ID NO: 2, and the amino acid sequence that is at least 95 percent identical to SEQ ID NO:2 and wherein the polypeptide retains plasma-membrane affinity;

wherein the molar ratio of the polypeptide to the inner leaflet component in the composition is in the range from 1:1 to 1:25;

in a pharmaceutically acceptable carrier;

(b) treating the ~~suspension of inner leaflet component and prosaposin related polypeptide~~ composition to form a nanovesicle;

wherein the nanovesicle formed has a diameter in the range 10 to 800 nm and exhibits anti-tumor activity.